UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/807,802	11/29/2001	James M. Wilson	GNVPN.031 USA	5849

270 7590 09/25/2003

HOWSON AND HOWSON
ONE SPRING HOUSE CORPORATION CENTER
BOX 457
321 NORRISTOWN ROAD
SPRING HOUSE, PA 19477

EXAMINER
WHITEMAN, BRIAN A

ART UNIT	PAPER NUMBER
1635	15

DATE MAILED: 09/25/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/807,802	WILSON ET AL.	
	Examiner	Art Unit	
	Brian Whiteman	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 July 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4,9-11,14,16-20,23-25 and 27-40* is/are pending in the application.

4a) Of the above claim(s) *9-11,14,17-20,29,30,37-40* is/are withdrawn from consideration.

5)☒ Claim(s) *33-36* is/are allowed.

6)☒ Claim(s) *1,2,4,16,23-25,27,28,31,32* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *3* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Non-Final Rejection

Claims 1, 2, 4, 9, 10, 11, 14, 16-20, and 23-40 are pending examination.

The cancellation of claims 3, 5, 6, and 26 and the amendment to claims 2, 4, 16, 17, 24, 25, and 27-32 in paper in paper no. 14 is acknowledged and entered.

Priority

Applicant's claim for domestic priority under 35 U.S.C. 119(e) and 35 U.S.C. 120 is acknowledged. However, the provisional application and PCT/US99/25694 upon which priority is claimed fails to provide adequate support under 35 U.S.C. 112 for claims 16 and 31 of this application.

Claims 1, 2, 4, 23, 24, 25, 27, 28, 32, 33, 34, 35, and 36 have priority to the provisional application. In addition, a composition comprising a carrier and a virus comprising a recombinant vector comprising an AAV-1 inverted terminal repeat (ITR) sequence selected from the group consisting of (a) nt 1 to 143 of SEQ ID NO: 1; (b) nt 4576 to 4718 of SEQ ID NO: 1; a nucleic acid sequence complementary to (a) or (b); and (d) a functional fragment of (a), (b), or (c) has support under 35 U.S.C. 112.

However, a pharmaceutical composition comprising a carrier and a virus comprising a recombinant vector comprising an AAV-1 inverted terminal repeat (ITR) sequence selected from the group consisting of (a) nt 1 to 143 of SEQ ID NO: 1; (b) nt 4576 to 4718 of SEQ ID NO: 1; a nucleic acid sequence complementary to (a) or (b); and (d) a functional fragment of (a), (b), or

(c) does not have priority to the provisional application and the PCT application because the claims do not have support under 35 U.S.C. 112 for the following reasons:

The breadth of the claims embrace a pharmaceutical composition comprising a carrier and virus comprising the vector according to claim 2. In view of the specification, the only intended use of the claimed invention is for use in any gene therapy method. However, at the time the application was filed (11/5/98), the state of the art for gene therapy was considered unpredictable. The specification does not provide sufficient guidance or factual evidence for one skilled in the art to use the claimed embodiment in any therapeutic method.

Furthermore, and with respect to claims directed to a vector useful for gene therapy and directed to any treatment of a mammal; the state of the art, at the time application was filed, as exemplified Anderson et al., *Nature*, Vol. 392, pp. 25-30, April 1998, displays major consideration for any gene transfer or any DNA therapy protocol involve issues that include:

1) The type of vector and amount of DNA constructs to be administered,

2) The route and time course of administration, the sites of administration, and successful uptake of the claimed DNA at the target site;

3) The trafficking of the genetic material within cellular organelles, the rate of degradation of the DNA, the level of mRNA produced, the stability of the mRNA product, the amount and stability of the protein produced, and

4) What amount of the expressed proteins considered to be therapeutically effective for a DNA therapy method.

In addition, all of these issues differ dramatically based on the specific vector used, the route of administration, the animal being treated, therapeutically effective amount of the DNA, and the disease being treated.

Anderson teaches that gene therapy is a powerful new technology that still requires several years before it will make a noticeable impact on the treatment of disease, and that several major deficiencies still exist including poor delivery systems, both viral and non-viral, and poor gene expression after genes are delivered (pp. 25-30). Anderson further teaches that the reason for the low efficiency of gene transfer and expression in human patients is that we still lack the basis understanding of how vectors should be constructed what regulatory sequences are appropriated for which cell types (page 30, column 1, last paragraph). Furthermore, Verma, *Nature*, Vol. 389, pages 239-242, 1997, indicates that factors including the nature of the diseases and/or disorders, the nature of a DNA and/or target tissue, and a delivery system and/or amounts of the DNA complexes employed in the delivery system that would generate a therapeutic effect *in vivo* must be considered for any gene therapy method to be successful (page 238, columns 1 and 2).

The specification teaches delivering an AAV-1 vector or an AAV-2 vector comprising a promoter operably linked to a transgene selected from a lac Z gene, an Epo gene or an alpha antitrypsin gene to cells *in vitro*. The specification teaches delivering the vectors to wild-type mice. The specification does not provide any therapeutic examples. In addition, the specification does not teach how to reasonably extrapolate from expressing a transgene in a wild-type mouse to treating a mammal with any disease or disorder. The specification does not teach

what amount of protein expression is considered therapeutic or how to determine if a therapeutic level was achieved using the claimed vector.

As a result, it is not apparent how one skilled in the art determines, without undue experimentation, which of the claimed recombinant vectors generates a therapeutic effect, how is it apparent as to how one skilled in the art, without any undue experimentation, practices any gene therapy method as contemplated by the claims, particularly given the unpredictability of gene therapy as a whole and/or the doubts expressed in the art of record.

Thus, for the reasons set forth above claims 16 and 31 only have priority to 11/29/01.

Election/Restrictions

Applicant's election with traverse of Group I (claims 1, 2, 4, 16, 23-25, 27, 28, and 31-36) in Paper No. 14 is acknowledged. The traversal is on the ground(s) that the international authority did not make a lack of unity and that AAV-1 sequences are the linking technical feature. This is not found persuasive for reasons of the lack of unity, see paper no. 13 filed 6/6/03. The technical feature linking the inventions of groups I-VI does not constitute a special technical feature as defined by PCT Rule 13.2, as it does not define a contribution over the prior art.

The requirement is still deemed proper and is therefore made FINAL.

Claims 9, 10, 11, 14, 17, 18, 19, 20, 29, 30, and 37-40 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in Paper No. 14.

Information Disclosure Statement

The applications (BR-BZ) listed on the 1449 have been considered but were not initialed on the 1449 because the applications are not considered published documents. See MPEP 609.

Specification

This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required. The WO cover sheet from the PCT is not considered an abstract on a separate sheet.

The use of the trademark AMERICAN TYPE CELL CULTURE (page 12, line 23; page 14, line 23) has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner, which might adversely affect their validity as trademarks.

Claim Objections

Claims 27 and 28 are objected to because of the following informalities: the term "a recombinant vector according to claim" is an improper dependent phrase. Suggest replacing the term with -- the recombinant vector according to claim --. Appropriate correction is required.

Applicants are advised that should claim 16 be found allowable, claim 31 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 16, 31, and 32 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a composition comprising a carrier and a virus comprising a recombinant vector comprising an AAV-1 inverted terminal repeat (ITR) sequence selected from the group consisting of (a) nt 1 to 143 of SEQ ID NO: 1; (b) nt 4576 to 4718 of SEQ ID NO: 1; a nucleic acid sequence complementary to (a) or (b); and (d) a functional fragment of (a), (b), or (c) and a transgene operably linked to a promoter, does not reasonably provide enablement for a pharmaceutical composition comprising a vector comprising an AAV-1 ITR lacking a promoter and a transgene. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

> Factors to be considered in determining whether a disclosure would require undue experimentation have been summarized in In re Wands, 858 F.2d 731, 8USPQ2d 1400 (Fed. Cir. 1988). They include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

Furthermore, and with respect to claims directed to a pharmaceutical composition comprising a virus comprising a vector and a suitable carrier useful for gene therapy and directed to any treatment of a mammal; the state of the art, at the time application was filed, as exemplified Anderson et al., *Nature*, Vol. 392, pp. 25-30, April 1998, displays major consideration for any gene transfer or any DNA therapy protocol involve issues that include:

1) The type of vector and amount of DNA constructs to be administered,

2) The route and time course of administration, the sites of administration, and successful uptake of the claimed DNA at the target site;

3) The trafficking of the genetic material within cellular organelles, the rate of degradation of the DNA, the level of mRNA produced, the stability of the mRNA product, the amount and stability of the protein produced, and

4) What amount of the expressed proteins considered to be therapeutically effective for a DNA therapy method.

In addition, all of these issues differ dramatically based on the specific vector used, the route of administration, the animal being treated, therapeutically effective amount of the DNA, and the disease being treated.

Anderson teaches that gene therapy is a powerful new technology that still requires several years before it will make a noticeable impact on the treatment of disease, and that several major deficiencies still exist including poor delivery systems, both viral and non-viral, and poor gene expression after genes are delivered (pp. 25-30). Anderson further teaches that the reason for the low efficiency of gene transfer and expression in human patients is that we still lack the

basis understanding of how vectors should be constructed what regulatory sequences are appropriated for which cell types (page 30, column 1, last paragraph). Furthermore, Verma, *Nature*, Vol. 389, pages 239-242, 1997, indicates that factors including the nature of the diseases and/or disorders, the nature of a DNA and/or target tissue, and a delivery system and/or amounts of the DNA complexes employed in the delivery system that would generate a therapeutic effect *in vivo* must be considered for any gene therapy method to be successful (page 238, columns 1 and 2). Thus, at the time the application was filed, gene therapy was considered unpredictable.

The specification teaches delivering an AAV-1 vector or an AAV-2 vector comprising a promoter operably linked to a transgene selected from a lac Z gene, an Epo gene or an alpha antitrypsin gene to cells *in vitro*. The specification teaches delivering the vectors to wild-type mice. The specification does not provide any therapeutic examples. In addition, the specification does not teach how to reasonably extrapolate from expressing a transgene in a wild-type mouse to treating a mammal with any disease or disorder. The specification does not teach what amount of protein expression is considered therapeutic or how to determine if a therapeutic level was achieved using the claimed vector.

Furthermore, with respect to claims 16, 31, and 32, the claims are directed to delivering the claimed vector to a host cell. In view of the art of record and specification, one skilled in the art would determine that the only use for the vector is for delivering a transgene to a host cell for expressing the transgene product. However, the claims comprise using a recombinant vector comprising no promoter or transgene just an AAV-1 ITR sequence. The specification provides sufficient guidance for one skilled in the art to make and use a recombinant vector comprising a 5' AAV ITR and a 3' AAV ITR and a promoter operatively linked to a transgene. However, the

specification fails to provide sufficient guidance or factual evidence for one skilled in the art to use a recombinant vector comprising no regulatory element that is not operatively linked to any specific transgene in the vector. The teachings in the specification are directed to using a promoter to express a transgene in a host cell. The as-filed specification provides guidance or evidence for how to make and use vectors comprising a 5' ITR and a 3' ITR and a promoter operatively linked to a transgene to direct transgene expression, however the claims do not recite such a structural limitation. Thus, to the extent the claims fail to recite distinguishing features to commensurate with the level of guidance presented, the claims are not considered enabled.

Furthermore, with respect to a pharmaceutical composition (claims 16 and 31), the claims are not considered enabled. In view of the In Re Wands Factors, the specification does not teach one skilled in the art how to use a pharmaceutical composition comprising the claimed vector. The claims embrace treating any diseases using a pharmaceutical composition comprising a virus comprising a suitable carrier and a vector comprising an AAV-1 ITR. At the time the application was filed, the art of record teaches several problems with gene therapy (See Anderson, Verma, and Orkin et al., ("Report and Recommendations of the Panel to Assess the NIH investments in Research on Gene Therapy", issued by the National Institute of Health, December 7, 1995). Orkin teaches, "Clinical efficacy has not been definitively demonstrated at this time in any gene therapy protocol" (page 1). The art of record teaches that significant problems in all basic aspects of gene therapy. In view of the art of record, the specification does not teach one skilled in the art how to practice the claimed embodiment.

As a result, it is not apparent how one skilled in the art determines, without undue experimentation, which of the claimed recombinant vectors generates a therapeutic effect, how is

it apparent as to how one skilled in the art, without any undue experimentation, practices any gene therapy method as contemplated by the claims, particularly given the unpredictability of gene therapy as a whole and/or the doubts expressed in the art of record.

In conclusion, the as-filed specification and claims coupled with the state of the art at the time the invention was made provide enablement for making and using a composition comprising a carrier and a virus comprising a recombinant vector comprising an AAV-1 inverted terminal repeat (ITR) sequence selected from the group consisting of (a) nt 1 to 143 of SEQ ID NO: 1; (b) nt 4576 to 4718 of SEQ ID NO: 1; a nucleic acid sequence complementary to (a) or (b); and (d) a functional fragment of (a), (b), or (c) and a transgene operably linked to a promoter. However, the rest of the disclosure encompassing a vector comprising no promoter or transgene is not considered enabled for the reasons set forth above. Given that making a recombinant vector comprising no promoter in the recombinant vector was unpredictable at the time the invention was made, and given the lack of sufficient guidance for making and using a pharmaceutical composition comprising the recombinant vector, one skilled in the art would have to engage in a large quantity of experimentation in order to practice the full scope of the claimed invention based on the applicants' disclosure and the unpredictability of gene therapy at the time the application was filed.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 23 and 32 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 23 recites the limitation "a selected gene product". There is insufficient antecedent basis for this limitation in the claim.

Claim 23 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted element is: a selected gene product. Claim 23 is directed to transfecting a mammalian cell with the molecule according to claim 1 to express a gene product. However the molecule of claim 1 does not contain a gene product

Claim 32 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential elements, such omission amounting to a gap between the elements. See MPEP § 2172.01. The omitted element is: a transgene. Claim 32 is directed to delivering a transgene using a host cell comprising a recombinant virus comprising a recombinant vector according to claim 2. However, the recombinant vector of claim 2 does not contain a transgene.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
(e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371(c) of this title before the invention thereof by the applicant for patent.

The changes made to 35 U.S.C. 102(e) by the American Inventors Protection Act of 1999 (AIPA) and the Intellectual Property and High Technology Technical Amendments Act of 2002 do not apply when the reference is a U.S. patent resulting directly or indirectly from an international application filed before November 29, 2000. Therefore, the prior art date of the reference is determined under 35 U.S.C. 102(e) prior to the amendment by the AIPA (pre-AIPA 35 U.S.C. 102(e)).

Claims 1 and 27 are rejected under 35 U.S.C. 102(a) as being anticipated by Rutledge et al. (IDS, Journal of Virology, Vol. 72, January 1998, pages 309-319). Rutledge teaches an AAV6 nucleic acid sequence that is complementary to applicants' SEQ ID NO: 1 (pages 309 and 312). Rutledge teaches infecting cells with the AAV6 nucleic acid (page 310).

Claims 1 and 27 are rejected under 35 U.S.C. 102(b) as being anticipated by Rose et al., (Microbiology, Vol. 546, 1966, pages 86-92). Rose teaches an AAV serotype 1 (AAV-1) that is a DNA sequence complementary to applicants' SEQ ID NO: 1 (page 86). Rose teaches a cell line infected with the AAV-1 (page 86).

Claims 1, 2, 4, 16, 24, 27, 28, and 31 are rejected under 35 U.S.C. 102(b) as being anticipated by Natsoulis et al., (US Patent 5,622,856, cited on a previous PTO-892). Natsoulis teaches using an AAV vector derived from AAV-1 (column 6, lines 8-21) that is a DNA sequence complementary to applicants' SEQ ID NO: 1, including nucleotides 1 to 143 of SEQ ID NO: 1 and nucleotide 4576 to 4718 of SEQ ID NO: 1. Natsoulis teaches that nucleotide sequence of AAV ITR regions are known (column 5, line 56). The AAV ITR may be derived from any of several AAV serotypes including AAV-1 (column 5, lines 55-67). Natsoulis teaches that the AAV vectors can include control sequences (column 6, lines 59-65). Natsoulis teaches transfecting a cell with the AAV vector (column 10, lines 39-56).

Claims 1, 2, 16, 23, 27, 28, 31, and 32 are rejected under 35 U.S.C. 102(e) as being anticipated by Russell et al., (US Patent 6,156,303). Russell teaches a nucleic acid sequence as set forth in SEQ ID NO: 2 or a nucleic acid sequence complementary to SEQ ID NO: 2 that is 67.9% (column 71, lines 9-11) identical to applicants' SEQ ID NO: 1. Russell further teaches SEQ ID NO: 2 comprising nucleotides 4683-4542, which are 97.1% identical to nucleotides 1-142 of applicants' SEQ ID NO: 1 and 85% identical to nucleotides 4576-4718 of applicants' SEQ ID NO: 1. Russell further teaches a cell comprising a vector comprising nucleotides 4683-4542 of SEQ ID NO: 2 and a heterologous nucleic acid sequence (column 71, lines 34-57).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 2 and 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Natsoulis et al., (US Patent 5,622,856) taken with Wilson et al. (WO 9613598).

Natsoulis teaches using an AAV vector derived from AAV-1 (column 6, lines 8-21) that is a DNA sequence complementary to applicants' SEQ ID NO: 1, including nucleotides 1 to 143 of SEQ ID NO: 1 and nucleotide 4576 to 4718 of SEQ ID NO: 1. Natsoulis teaches that nucleotide sequence of AAV ITR regions are known (column 5, line 56). The AAV ITR may be derived from any of several AAV serotypes including AAV-1 (column 5, lines 55-67).

However, Natsoulis does not specifically teach a recombinant vector according to claim 2, wherein said vector further comprises adenovirus sequences.

However, at the time the invention was made, Wilson teaches a hybrid adenovirus vector comprising AAV ITRs and a portion of an adenovirus (abstract). Wilson teaches production of the vector to overcome many of the limitations of prior art viral vectors, e.g., ability to provide extremely high levels of transgene delivery to virtually all cell types and the ability to provide stable long-term transgene integration into the host cell (page 8).

It would have been *prima facie* obvious to a person of ordinary skill in the art at the time the invention was made to combine the teaching of Natsoulis taken with Wilson, namely to produce a hybrid vector comprising 5' and 3' AAV-1 ITRS and adenovirus sequences. One of ordinary skill in the art would have been motivated to produce the vector to overcome the limitations of prior art viral vectors.

Therefore the invention as a whole would have been *prima facie* obvious to one ordinary skill in the art at the time the invention was made.

Conclusion

Claims 33-36 are in condition for allowance because the claims are free of the prior art of record.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Brian Whiteman whose telephone number is (703) 305-0775.

The examiner can normally be reached on Monday through Friday from 7:00 to 4:00 (Eastern Standard Time), with alternating Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John L. LeGuyader, SPE - Art Unit 1635, can be reached at (703) 308-0447.

Papers related to this application may be submitted to Group 1600 by facsimile transmission. Papers should be faxed to Group 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center number is (703) 872-9306.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Brian Whiteman
Patent Examiner, Group 1635

Scott D. Priebe

SCOTT D. PRIEBE, PH.D
PRIMARY EXAMINER